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Risk factors in Central Poland for the development of superficial and nodular basal cell carcinomas

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Abstract

Introduction: In the last decades the number of skin carcinomas has dramatically increased, which is mainly connected with changes in lifestyle, especially with common use of artificial light sources such as sunbeds. Basal cell carcinoma (BCC) is the most common form of skin cancer in white populations. Basal cell carcinomas are divided into subtypes, depending on their clinical picture and histology. The main groups are nodular (nBCC) and superficial (sBCC) ones. The major recognized risk factors for basal cell carcinoma (BCC) are exposure to chronic and intermittent burning doses of sunlight. Other risk factors leading to the development of the nBCC and sBCC subtypes of BCC are not well established.

Material and methods: An analysis of 123 patients with either nBCC or sBCC, living in Lodz, Poland, regarding various intrinsic and environmental parameters was undertaken following the histological diagnosis of BCC.

Results: No statistical differences were observed between the BCC subtype and sex, age, hair colour, eye colour, smoking, family history of skin cancer, occupation, or past episodes of sunburn. While sBCCs tended to occur on unexposed body sites in phototype I/II subjects who mainly avoided direct sunlight, nBCCs tended to occur on sun-exposed body sites in phototype III subjects who were frequently in direct sunlight.

Conclusions: Thus the development of particular BCC subtypes is partially dependent on phototype and personal sun behaviour.

Key words: nodular basal cell carcinoma, skin phototype, sun exposure, superficial basal cell carcinoma.

Introduction

Basal cell carcinoma (BCC) is the most common form of skin cancer in white populations, with an average lifetime risk of developing BCC estimated at approximately 30% [1]. In general, the closer subjects live to the equator, the higher the incidence [2]. Sun exposure is a major risk factor for all BCCs [3], although the pattern of irradiation may be different for the various subtypes [4, 5]. Intermittent intense sun exposure leading to sunburn episodes, especially during childhood and adolescence, is a consistent finding [6]. Cumulative sun exposure is likely to be an important additional risk factor [7]. Individuals with the highest risk of developing BCCs are usually fair-skinned and have a history of burning rather than tanning in response to solar ultraviolet radiation [8].

In several countries worldwide there has been a considerable increase in the incidence of BCCs in recent years. The highest increase in incidence rate is reported in Australia and is 1-2% annually [9]. In the south-east Netherlands, an approximate doubling in BCC incidence from 2000 to 2015 is projected, due, in part, to ageing of the population [10]. In Poland there is a lack of statistical data concerning the prevalence of BCC but regional data from the north of the country indicate a recent increase in the incidence rate. The number of BCC cases is thought to be significantly under-reported as the lesions are often removed after clinical diagnosis but without histological analysis, and patient management is frequently undertaken by general practitioners in primary care rather than by dermatologists [11, 12]. In most European countries, BCCs are not included in national cancer registries so an accurate picture of BCC prevalence and any change in incidence over time is difficult to obtain.

The BCCs are divided into subtypes, depending on their histology, with the two main groups being nodular (nBCC) and superficial (sBCC) [13]. Nodular BCC is considered as non-aggressive while the other subtypes are associated with an increased risk of recurrence or local invasive behaviour. Other differences are reported. For example, patients with sBCC are generally younger than patients with nBCC, the frequency of BCC is higher overall in men than in women but the frequency of sBCC is higher in women than in men, and BCCs on the head/neck are mainly nodular while those on the trunk are mainly superficial [13-15]. Because of these variables, BCC should not be considered as a single entity and identification of the risk factors involved in development of the subtypes may aid in the management of these lesions, which represent a significant and costly health burden as well as considerable cosmetic disfigurement.

The aim of the present study was to obtain information, by use of a questionnaire, about various personal and environmental risk factors in patients living in Lodz, central Poland, who had been diagnosed with either sBCC or nBCC.

Material and methods

The total number of patients biopsied and treated for a single BCC at the Department of Dermatology, Medical University of Lodz, between 2000 and 2006 was 445. A letter of invitation was sent to these individuals inviting them to participate in the study and 123 accepted. They were all Caucasian (53 M, 70 F, mean age 68 years, range 49-86 years) and none was an organ transplant recipient, was being treated with immuno-suppressive drugs or suffered from any other malignancy. Each subject gave written informed

consent before entering the study which had been approved by the local Ethic Committee.

The individuals were given a questionnaire to complete which asked for details of sex, age, body site of BCC, hair colour ("fair" included red, blond and dark blond, and "dark" included brown and black), eye colour ("pale" included blue, grey and green, and "dark" included brown and black), smoking history, occupation, amount of time spent outside (hobbies, sport or work), frequency of sun exposure, use of sunbeds, number of lifetime sunburns, ability to tan in response to sunlight, and family history of skin cancer. In addition the subjects were assessed by a dermatologist for their skin phototype, according to the Fitzpatrick score [16]. They were assigned to phototype I/II (always sunburns, never or rarely tans, lack of or weak immediate and delayed pigmentation, and ivory white or white skin on unexposed body site), III (sometimes burns, always tans, visible immediate and delayed pigmentation and white skin on unexposed body site) or IV (never burns, always tans, moderate immediate or delayed pigmentation, moderate tan on unexposed body site). The results were analysed statistically by the Mann-Whitney and the χ^2 tests, with $p < 0.05$ considered as being significant.

Results

The results, based on the questionnaire, were analysed in relation to the histological diagnosis of sBCC or nBCC and are shown in Table I. The histology of the two types of lesions are illustrated in Figure 1. The superficial subtype of BCC was diagnosed in 22.7% of the 123 patients and nBCC in 77.3%. The mean diameter of the nBCCs was 0.9 cm (range 0.3-1.5 cm) and of the sBCCs was 2.5 cm (range 0.5-7.0 cm) ($p < 0.05$). There was no statistical difference in the size of either of the two subtypes in men compared with women. There was no correlation between the histological subtype of BCC and the sex, age, hair colour, eye colour, smoking history, family history of skin cancer or outdoor activities of the patient ($p > 0.05$ for all comparisons). In addition no significant difference was found between subtype and frequency of exposure to the sun during work, sport or hobbies ($p > 0.05$). The patients were asked whether they had been sunburnt at any time and, if so, on how many occasions. There was no correlation between the BCC subtype and the occurrence or lack of occurrence of sunburn during a lifetime ($p > 0.05$). It was found that the subjects who said that they had experienced sunburn could not recall on how many occasions during their lifetime this had happened. Thus they were divided into those who reported a single sunburn episode and those who reported more than one sunburn episode (Table I).

Table I. Characteristics of patients diagnosed with either superficial or nodular basal cell carcinoma (BCC)

	Superficial BCC	Nodular BCC
Number of subjects	28	95
Mean age [years]	69	65
Sex	F 18, M 10	F 51, M 44
Hair colour	fair 18, dark 10	fair 62, dark 33
Eye colour	pale 15, dark 13	pale 56, dark 39
Smoking history	yes 14, no 14	yes 48, no 47
Family history of skin cancer	yes 17, no 11	yes 46, no 49
Outdoor activities	yes 15, no 13	yes 57, no 43
Exposure to the sun	frequent 13, rare 15	frequent 57, rare 38
Occurrence of sunburn	yes 12: 5 on one occasion, 7 on multiple occasions	yes 47: 25 on one occasion, 22 on multiple occasions
Number with skin phototype	I/II 13, III 9, IV 6	I/II 22, III 52, IV 21
Sunbed users	yes 1 (phototype III), no 27	yes 3 (phototype III), no 92
Body site of BCC	sun exposed 3, unexposed 25	sun exposed 66, unexposed 29

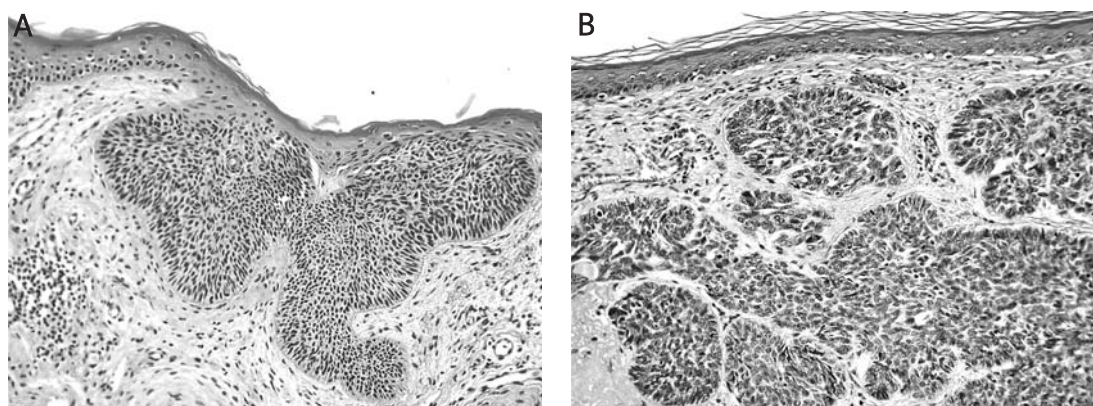


Figure 1. Histology of (A; mag. 200×) superficial (buds of basaloid cells attached to the undersurface of the epidermis, nests of various sizes in the upper dermis, tumour cell aggregates with typical peripheral palisading) and (B; mag. 200×) nodular (tumour cells with large, hyperchromatic, oval nuclei and sparse cytoplasm, various size of tumour nests, tumour cells align more densely in a palisade pattern at the periphery of these nests) subtypes of basal cell carcinoma

On analysis, no significant difference between the subtype of BCC and sunburn episodes was demonstrated ($p > 0.05$). When skin phototype was considered, it was revealed that sBCC occurred more frequently in those with phototype I/II than III or IV, and nBCC more frequently in those with phototype III than I/II or IV ($p < 0.05$ for both comparisons) (Figure 2). In 56% of patients the BCCs were located on sun-exposed body sites. Nodular BCCs were found more frequently (69.5%) on sun-exposed areas (mainly the head and neck) than on unexposed areas ($p < 0.005$), while more sBCCs (89.3%) were present on unexposed areas (the trunk) than on sun-exposed areas ($p < 0.005$) (Figure 3). There was no difference between males and females in the distribution of either nBCCs or sBCCs ($p > 0.05$ for both comparisons). The number

of sunbed users was too small (Table I) to allow statistical analysis.

Discussion

During the seven-year period from 2000 to 2006, 445 new cases of BCC were diagnosed and treated in the Dermatology Department, Medical University of Lodz. Although this number represents an unknown proportion of the total number of BCCs in central Poland, a doubling in the annual incidence rate at our hospital was noted, from 46 cases in 2000 to 96 in 2006. This trend follows that noted in many other reports worldwide, such as in Britain [17], Brazil [18], Sweden [19], the Netherlands [10], Italy [20] and Australia [19]. Most studies indicate a higher risk for BCC development in the elderly,

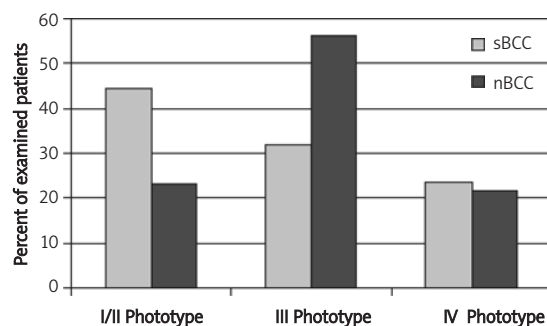


Figure 2. Phototype of the 123 patients who had either nodular (n) or superficial (s) subtype of basal cell carcinoma

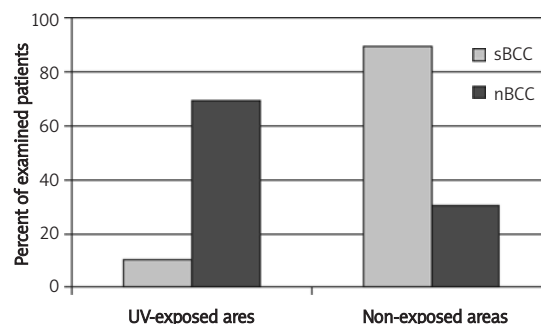


Figure 3. Body sites of the nodular (n) and superficial (s) basal cell carcinomas in 123 patients

although an increase in the number of cases in younger women has been noted recently [10, 17, 21]. This was not the case in our population, as the mean age of BCC cases in 2000 was 69.2 years (24 cases in women and 22 in men) and in 2006 was 68.8 years (50 cases in women and 46 in men). Basal cell carcinoma is reported to be more common in men than in women with a male : female ratio often quoted as around 2 : 1 [13, 15, 22, 23]. In other studies the incidence in women is not significantly different from that in men [4, 25-28] and our findings fit with the latter results as only slightly more than half (56%) of the total BCCs occurred in women.

When the subtypes of BCC were analysed histologically, nBCC was found in the majority (77.3%) of cases. This result is consistent with the observations made by others [13, 24, 29], although in some surveys sBCCs outnumber nBCCs [reviewed in 25]. This discrepancy may be due to the method of collecting the BCC cases, as many sBCCs are treated outside a hospital setting and are not analysed histologically, thus leading to a smaller proportion than is actually present in the community. The size of the sBCCs was significantly larger than the size of the nBCCs in our study. This may be explained by the sBCCs not being recognised clinically until a later stage than is the case for the nBCCs.

We were interested to try to relate age and sex to the occurrence of the subtypes of BCC, as an increasing incidence of sBCC in younger subjects, especially women, has been reported in the last decade [4, 24]. However, although we found that 64% of the cases of sBCC were in women, this was not a significant difference from nBCC, perhaps due to the relatively small number of patients studied. In addition there was no age difference between those individuals developing sBCC (mean age of women 68.2 years, men 70.8 years) and nBCC (mean age of women 66.1 years, men 64.9 years), unlike other reports where sBCC was diagnosed at a significantly lower age than in those with nBCC

[4, 13, 24]. Several groups have found that fair hair and pale eyes are risk factors for BCC [14, 30]. In the present study we demonstrated that the majority of the patients with BCC had fair hair and pale eyes, but having these features did not correlate significantly with the development of sBCC or nBCC. Similarly, there was no correlation of BCC subtype with smoking history or a family history of BCC.

As cumulative and intermittent intense sun exposure are recognized as the most important environmental risk factors for BCC, the involvement of the sun in the development of BCC subtypes was examined in several ways, by asking first whether the patient's job was outdoors or indoors, secondly how much time the patients spent outside as a result of their hobbies or sport, and thirdly whether the patient remembered experiencing one or more sunburn episodes in the past. In no case was there a significant difference between these factors and the occurrence of sBCC or nBCC. However, individuals with sBCC were less likely to expose themselves frequently to the sun than those with nBCC and, when skin phototype was considered, sBCC occurred most often in subjects with phototype I/II and nBCC in subjects with phototype III, indicating that the response of the individual to sun exposure may be a factor in determining the subtype of BCC that develops. Basal cell carcinomas have been reported to occur predominantly in those with phototype I/II, but the risk of nBCC or sBCC according to phototype has not been recorded previously. Basal cell carcinomas are found on body sites that are infrequently sun-exposed as well as on chronically exposed skin, and the sites most commonly involved differ for the subtypes, with nBCC developing mainly on the head and neck and sBCC mainly on the trunk [4, 27, 29, 31]. This was confirmed in the present study, with almost 70% of nBCCs on sun-exposed areas (head and neck) and 89% of sBCCs on less sun-exposed areas (trunk). We found that the majority of the nBCC patients tended to expose themselves frequently to the sun, while the majority of the

sBCC patients tended to avoid sun exposure. This behavioural difference may be explained to some extent by phototype, as 46% of the sBCC patients, but only 23% of the nBCC patients, were phototype I/II. In contrast, Neale *et al.* [15] reported a positive association between sun sensitivity and BCC of the head (predominantly nBCC), but this was absent for BCC of the trunk (predominantly sBCC). Their study was based in Nambour, Queensland, a location with much higher solar ultraviolet radiation than central Poland, and perhaps the difference in UV intensity and cumulative dose may be important variables in determining the subtype of BCC that develops and its body site. No significant difference in the site distribution of the BCC subtypes between men and women was demonstrated in our study group, a result also reported by Bernard *et al.* [25] but not by Bastiaens *et al.* [4], who found a slightly higher number of sBCCs on the trunk in males (55%) compared with females in a review that contained a larger number of patients with sBCC (302) than ours. While the use of sunbeds has been suggested as contributing to BCC induction (32), this was not an important factor in the present study, as only 3% of the individuals with BCC had used such tanning devices. Sunbeds are not popular in Poland and were not widely available in the last decades of the twentieth century.

In conclusion, our results reveal that, in central Poland, nBCCs tend to occur on exposed body sites in many subjects with phototype III who are frequently in direct sunlight, while sBCCs tend to occur on unexposed body sites in many subjects with phototype I/II who frequently avoid direct sunlight. Thus the development of the BCC subtype may be partially dependent on phototype and personal sun behaviour.

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